

polypeptide of the invention (claims 27-29) and a method to identify a synthetic endonuclease (claim 26).

Claims 2-3 and 30-33, which depend on claim 1, each recite an amino acid sequence for a peptide or polypeptide of the invention. In particular, SEQ ID NO:2 (claim 2; assigned to Group I) includes nucleic acid binding sequences of Engrailed and a consensus EF-Hand loop sequence (a metal binding domain); SEQ ID NO:3 (claim 3; assigned to Group II) includes  $\alpha 2$  and  $\alpha 3$  of Engrailed minus the last turn of  $\alpha 2$  and a  $\beta$  turn and calmodulin loop I (a metal binding domain); SEQ ID NO:4 (claim 30; assigned to Group III) includes  $\alpha 2$  and  $\alpha 3$  of Engrailed and a greater portion of calmodulin loop I than SEQ ID NO:3; SEQ ID NO:5 (claim 31; assigned to Group IV) includes  $\alpha 2$  and  $\alpha 3$  of Antennapedia and calmodulin loop III (a metal binding domain); SEQ ID NO:6 (claim 32; assigned to Group V) includes a calmodulin loop I modified Engrailed sequence; and SEQ ID NO:7 (see claim 33 above; SEQ ID NO:7 is similar to SEQ ID NO:2 except that position 24 is W not H). As each amino acid sequence recited in the claims was grouped separately, claim 33 would likely have been assigned to Group VIII along with claims 1, 4-18, and 27-29.

Figure 2 of the specification (a copy is enclosed herewith), which illustrates metal binding domains by shading, EF-Hand related sequences by a single underline, and nucleic acid binding sequences, e.g., homeodomains, by double underlining, shows the structural similarity of SEQ ID Nos:2-7. For example, all of SEQ ID NOs:2-7 have the motifs: DKDGN/DGT/Y/FL, TE/RRRR, and W/HFQN, and all but one has the motif: KIW/HFQNKRRARIK. Thus, the peptides of SEQ ID NOs:2-7, and in particularly the peptides of SEQ ID NOs:2-5 and 7, are, at the primary amino acid sequence level, structurally related.

Based on Applicant's disclosure, Applicant's Representatives propose the following groups of claims for election in a revised Restriction Requirement: claims 1-18 and 27-33 (group A), directed to a synthetic peptide or polypeptide of the invention and methods of using the synthetic endonuclease; claims 19-25 (group B), directed to an isolated nucleic acid molecule, expression cassette or vector encoding the peptide or polypeptide of the invention, or host cell comprising the expression cassette of the invention; and claim 26 (group C) directed to a method to identify a synthetic endonuclease.

In response to the Restriction Requirement mailed March 4, 2002, Applicant provisionally elects, with traverse, the claims of new Group VIII (claims 1, 4-18, 27-29, and 33), directed to an isolated synthetic peptide or polypeptide comprising a domain which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide or polypeptide comprises SEQ ID NO:7. Reconsideration and withdrawal of the restriction requirement, in view of the remarks herein, is respectfully requested.

The Restriction Requirement is traversed on the basis that the inventions are so closely related within the context of the disclosure of the application that they cannot properly be considered independent and distinct within the statutory meaning of 35 U.S.C. § 121. Claims directed to an isolated synthetic peptide or polypeptide comprising a domain which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide comprises SEQ ID NO:7 (TERRRQQLDKDGDGTIDEREIKIWFQNKRAKIK) and methods of using that peptide or polypeptide (claims 1, 4-18, 27-29 and 33; Group VIII) are clearly related to claims directed to an isolated synthetic peptide or polypeptide comprising a domain which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide comprises SEQ ID NO:2 (TERRRQQLDKDGDGTI DEREIKIHFQNKRAKIK) and methods of using that peptide or polypeptide (claims 1-2, 4-18, and 27-29); claims directed to an isolated synthetic peptide or polypeptide comprising a domain which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide comprises SEQ ID NO:3 (TERRRFDKDGNGYISAAELRHV KIWFQNKRAKIK) and methods of using that peptide or polypeptide (claims 1, 3-18 and 27-29; Group II); claims directed to an isolated synthetic peptide or polypeptide comprising a domain

which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide comprises SEQ ID NO:4 (TERRRFRVFDKDGNGYISAAEKIWFQNKEAKIK) and methods of using that peptide or polypeptide (claims 1, 4-18 and 27-30; Group III); claims directed to an isolated synthetic peptide or polypeptide comprising a domain which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide comprises SEQ ID NO:5 (TRRRRFSLFDKDGDGTITTKEEVWFQNRMKWK) and methods of using that peptide or polypeptide (claims 1, 4-18, 27-29, and 31; Group IV); claims directed to an isolated synthetic peptide or polypeptide comprising a domain which specifically binds a nucleic acid sequence and a domain which specifically binds a metal which is hydrolytic or redox active, wherein the domain which specifically binds the metal is within the domain which specifically binds the nucleic acid sequence, wherein the peptide comprises SEQ ID NO:6 (DEKRPRTAFSGEQLA RLKREFNENRYLTERRRLRVFDKDGNGFISAAEKIW FQNKRAKIKKST) and methods of using that peptide or polypeptide (claims 1, 4-18, 27-29 and 32; Group V).

The Restriction Requirement is also traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. Moreover, it is submitted that Applicant should not be required to incur the additional costs associated with the filing of multiple divisional applications in order to obtain protection for the claimed subject matter, e.g., five divisional applications in addition to the present application to obtain protection for six related sequences. Due to the relatedness of the subject matter of the claims in Group VIII and Groups I-V, as discussed above, the claims in Group VIII and Groups I-V can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. In particular, the claims in Groups I-V and VIII can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner as the claims in Groups I-V and

Group VIII (the claims of Group VIII are presumably classified in the same class and subclass as claims which include SEQ ID NO:2, as SEQ ID NO:2 has a single amino acid substitution relative to SEQ ID NO:7) are in the same class and subclass for search purposes.

Moreover, as each of the claims which recite a particular amino acid sequence (claims 2-3 and 30-33) are dependent on (linked to) claim 1, claims 1-18 and 27-33 should be examined in the same application. M.P.E.P. 809.03. Thus, the Restriction Requirement is properly traversed. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

Further, in the event the Examiner remains of the opinion that the restriction is proper as stated in the Restriction Requirement dated March 4, 2002, Applicant's Representatives respectfully request rejoinder of Groups I-V with Group VIII upon a notice of allowable subject matter for the claims in Group VIII.

The Examiner is invited to contact Applicant's attorney (612-373-6959) if there are any questions concerning this Response or if prosecution of this application may be assisted thereby.

Respectfully submitted,

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May 6, 2002

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 6<sup>th</sup> day of May, 2002. (Monday)

Candis B. Buending

Name

Signature